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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,535	05/31/2000	Jean-Christophe Francis Audonnet	454313-2335.1	6015

20999 7590 03/20/2002

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EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	14

DATE MAILED: 03/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/586,535	Applicant(s) AUDONNET ET AL.	
	Examiner Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13,15-26,28-35,37 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

The Amendment and Remarks filed on January 8, 2002 has been entered as Paper #13.

Election/Restrictions

In response to the restriction by original presentation of new claims 14, 27, 36, and 38 in Paper #12, Applicants argue that the restriction is improper, that new claim 14 provides the chemical structure that includes carbomer recited in claim 13; that claim 27 depend upon claim 20, which has been examined in the previous Office action. Applicants further cited *Allan et al* (USP 6,217,833) to support that there is no undue burden on the Examiner in search and examining the subject matter.

The arguments have been carefully considered but found not persuasive for the reason of record advanced in Paper #12 and the following.

Newly submitted claim 14 in Paper #10 presents a chemical structure of a polymer formula, which encompasses the carbomer in claim 13. However, the new formula also embraces structures beyond the carbomer of claim 13, thus, requires further search and consideration. Regarding the new claim 20, although original claim 11 recites "another porcine immunogen", it reads on any porcine immunogen including one of the ORF1, ORF2 of each of the PCV1 and PCV2, respectively. Newly submitted claim 20 has substantially changed the scope of the original claim 11 by excluding PCV1 and PCV2, therefore claim 20 will be examined to the extent that it reads on the

original claim 11. This point was only implicitly indicated in the prior Office action (Paper #12, page 2, 3rd paragraph), and therefore, will be explicitly pointed out in this Office action. Moreover, if applicants are willing to further pursue the subject matter, it is noted by the Office that among the long list of porcine pathogens recited in new claims 27 and 38, some have not even been discussed in the instant specification. Further, *Allan et al* could not provide support for the argument, because the restriction by original presentation is referred to the first Office action Paper #8, and *Allan et al* is not a prior art to the instant application.

Therefore, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of these inventions is not co-extensive. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 12-39 are pending, however, claims 14, 27, 36, and 38 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claim 20 will be examined to the extent that it reads on the original claim 11. Claims 12, 13, 15-26, 28-35, 37, and 39 are under current examination.

Priority

This application claims priority to U.S. provisional application 60/138,352, filed June 10, 1999.

The prior rejections of Paper #12 are withdrawn because *Allan et al* (USP 6,217,833) is not a prior art for the instant application.

New grounds of rejections appear below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 18-26, 37, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Poet et al* (US 6,287,856) as evidenced by *Meehan et al* (J Gen Virol 1998;79:2171-79), in view of *Eppstein et al* (US 4,946,787).

These claims are drawn to an immunogenic preparation comprising a complex of at least one plasmid encoding and capable of expressing in a porcine host an isolated nucleic acid molecule selected from the group consisting of ORF1 and ORF2 of PCV-I or PCV-II, or an immunogen from a porcine pathogenic agent, and an adjuvant comprising a cationic lipid formula. Claims 18, 19, and 37 are drawn to an additional

cytokine component in the plasmid, preferably GM-CSF. Claim 20 is drawn to an additional plasmid encoding a porcine pathogen. Claim 39 is drawn to a method comprising administering to a porcine host the immunogenic preparation.

Poet et al teach an immunogenic preparation (vaccine) comprising a nucleic acid encoding a porcine circovirus, particularly the ORF region of the PCV-I (column 5, lines 40-62), and using the DNA vaccine for inducing an immunological response comprising administering to a porcine said vaccine (Sections starting from line 55 of column 3, SEQ ID Nos: 1, 2, 20-32), which nucleic acids are preferably constructed in a plasmid (lines 56-61). *Poet et al* further teach that in addition to the PCV coding region, the construct could include cytokine-coding region, such as GM-CSF or IL-12 (column 4, lines 61-67) to bring out the specific level of immune response needed to protect the animal from the targeted disease. According to *Meehan et al* (abstract, right column in page 2176), the disclosed sequences (SEQ ID Nos: 1 & 2) of *Poet et al* are correspondent to ORF1 of PCV-I. *Poet et al* go on to teach that the DNA vaccines can be administered in combination with one or more DNA vaccine preparations for viral diseases such as porcine parvovirus (column 7, lines 57-67); and can be incorporated in liposomes to enhance *in vivo* transfection (column 8, lines 1-16, particularly line 14). *Poet et al* do not teach the adjuvant formula recited in claim 12.

Meehan et al teach the concept of PCV-I and PCV-II according to their relations with wasting syndromes in pigs. They provide the genome characterization of PCV-I and PCV-II, including analysis of ORFs. For example, they teach ORF1 of PCV is responsive for encoding major structural protein (right column in page 2177).

Eppstein et al teach a "formula I", which is embraced by the formula of claim 12. They teach to improve recombinant viral vector delivery by using formula I (column 3), "THE MOST DESIRABLE TRANSFECTION METHOD WOULD INVOLVE ONE THAT GIVES VERY HIGH EFFICIENCY WITHOUT THE INTRODUCTION OF ANY TOXIC OR INFECTIOUS SUBSTANCES AND BE SIMPLE TO PERFORM WITHOUT A SOPHISTICATED APPARATUS. THE METHOD THAT WE DESCRIBE SATISFIES ALL OF THESE CRITERIA".

Evidently, PCV ORFs could be used as a DNA vaccine for porcine disease is well known in the art, such DNA vaccine could be administered in combination with cytokines and a cationic lipid, such as formula of claim 12, or with other porcine pathogen vaccines, are also well known in the art. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Poet et al*, by simply including one of the liposome adjuvant, such as formula I of *Eppstein et al* with a reasonable expectation of success. One of skilled in the art would have been motivated to do so, because an enhanced vector transfection *in vivo,* would lead to an enhanced vaccine effect. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 13, 18-26, 37, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Poet et al* (US 6,217,883) in view of *Neurath et al* (US 6,165,493).

Claim 13 is drawn to an immunogenic preparation comprising a complex of at least one plasmid encoding and capable of expressing in a porcine host an isolated nucleic acid molecule selected from the group consisting of ORF1 and ORF 2 of PCVII,

or an immunogen from a porcine pathogenic agent other than PCV-2 or PCV-1, and an adjuvant comprising a carbomer.

Poet et al teach an immunogenic preparation (vaccine) comprising a plasmid encoding a porcine circovirus ORF of either PCV-I or PCV-II, which can be administered in combination with one or more DNA vaccine preparations for viral diseases such as porcine parvovirus or herpes virus. *Poet et al* further teach that in addition to the PCV-coding region, the construct could include cytokine-coding region, such as GM-CSF, to bring out the specific level of immune response needed to protect the animal from the targeted disease. *Poet et al* go on to teach that (column 7, lines 57-67); and can be incorporated in liposomes to enhance *in vivo* transfection (column 8, lines 1-16, particularly line 14), *Poet et al* do not teach a carbomer adjuvant.

Neurath et al teach methods and compositions for viral vaccine using recombinant viral particles and an adjuvant. They teach a vaccine preparation mixture comprising a carbomer (column 28).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Poet et al*, by simply including a carbomer adjuvant in their vaccine preparation, as taught by *Neurath et al* with a reasonable expectation of success. One of skilled in the art would have been motivated to do so with any cationic lipid of choice because an enhanced vector transfection *in vivo* would lead to an enhanced vaccine effect. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary..

Claims 12, 15-26, 28-35, 37, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Poet et al* (US 6,217,883) and *Eppstein et al* (US 4,946,787) as applied to claims 12, 18-26, 37, and 39 above, further in view of *Nabel. et al* (US 5,910,488).

These claims are drawn to an immunogenic preparation comprising a complex of at least one plasmid encoding and capable of expressing in a porcine host an isolated nucleic acid molecule selected from the group consisting of ORF1 and ORF 2 of PCVII, or an immunogen from a porcine pathogenic agent, and an adjuvant comprising a cationic lipid of DMRIE; wherein DMRIE is coupled to DOPE or a neutral lipid, wherein the optimal ratio of DMRIE:DOPE ranges from 95:5 to 5:95.

Poet et al teach an immunogenic preparation (vaccine) comprising a nucleic acid encoding a porcine circovirus ORF1, which nucleic acids are preferably constructed in a plasmid (lines 56-61). *Poet et al* further teach that in addition to the PCV coding region, the construct could include cytokine-coding region, such as GM-CSF, to bring out the specific level of immune response needed to protect the animal from the targeted disease. *Poet et al* go on to teach that the DNA vaccines can be administered in combination with one or more DNA vaccine preparations for viral diseases such as porcine parvovirus (column 7, lines 57-67); and can be incorporated in liposomes to enhance *in vivo* transfection (column 8, lines 1-16, particularly line 14), *Poet et al* and *Eppstein et al* do not teach DMRIE coupled to DOPE as an adjuvant.

Nabel et al teach a method for gene delivery including a plasmid complexes with cationic liposomes, which may be prepared from a mixture of positively charged

(DMRIE) and negatively charged lipids, neutral lipids (DOPE) and cholesterol or similar sterol, the preferred ratio of DMRIE to DOPE is 9:1 to 1:9, which is encompassed by the instant claims (columns 15 & 16). They further teach that such DMRIE/DOPE formulation shows up to 7 fold increase in transfection efficiency (example 6), and does not aggregate at high concentrations, allow for introducing 100-1000 times more DNA which could markedly improve gene expression *in vivo* (lines 16-23 of column 16), which anticipates the ranges in the instant claims (95:5-5:95). Even if *Nabel et al* do not teach the particular plasmid:DMRIE weight ratios recited in the instant claims, the experimentation to obtain these ratios are considered as routine to optimize the delivery condition.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Poet et al*, by simply including a DMRIE/DOPE adjuvant as taught by *Nabel et al,* with a reasonable expectation of success. One of skilled in the art would have been motivated to do so, because DMRIE/DOPE adjuvant could enhance the capability and efficiency in gene transfection *in vivo,* thus an enhanced vaccine effect. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
March 12, 2002

JAMES KETTER
PRIMARY EXAMINER